Amendments to the Claims

This listing of claims will replace all prior versions, and listings of claims in the application.

1. (currently amended) A biologically active polypeptide having the amino acid sequence consisting essentially of AlaValAlaGluIleGlnLeuMetHisX₀₁X₀₂X₀₃LysX₀₄ (SEQ ID NO:1), wherein:

 X_{01} is Ala, Asp or Gln;

X₀₂ is Leu, Arg or homoArg;

X₀₃ is Arg or Ala; [[and]]

X₀₄ is Phe or Trp; and

wherein said polypeptide has a biological activity substantially similar to the biological activity of parathyroid hormone.

- 2. (cancelled).
- 3. (withdrawn) A polypeptide comprising an amino acid sequence consisting essentially of AlaValAlaGluIleGlnLeuMetHisX₀₁ArgAlaLysX₀₂ (SEQ ID NO:2), wherein:

 X_{01} is Ala, Asp or Gln; and

 X_{02} is Trp or His.

4. (withdrawn) A polypeptide having an amino acid sequence that is at least 85% identical to the amino acid sequence of the polypeptide of claim 3.

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5. (withdrawn) A polypeptide comprising the amino acid sequence: AlaValAla GluIleGlnLeuMetHisX₀₁X₀₂X₀₃LysX₀₄LeuAsnSerMetX₀₅Arg (SEQ ID NO:25), AlaValAla GluIleGlnLeuMetHisX₀₁X₀₂X₀₃LysX₀₄LeuAsnSerMetX₀₅ArgValGlu (SEQ ID NO:26), AlaValAlaGluIleGlnLeuMetHisX₀₁X₀₂X₀₃LysX₀₄LeuAsnSerMetX₀₅ArgValGluTrpLeu (SEQ ID NO:27) AlaValAlaGluIleGlnLeuMetHisX₀₁X₀₂X₀₃LysX₀₄LeuAsnSerMetX₀₅ArgValGluTrpLeuArgLys (SEQ ID NO:28), AlaValAlaGluIleGlnLeuMetHisX₀₁X₀₂X₀₃LysX₀₄LeuAsnSerMetX₀₅ArgValGluTrpLeuArgLysLysLeu (SEQ ID NO:29), AlaValAlaGluIleGlnLeuMetHisX₀₁X₀₂X₀₃LysX₀₄LeuAsnSerMetX₀₅ArgValGluTrpLeuArgLysLysLeuGlnAsp (SEQ ID NO:30), or AlaValAlaGluIleGlnLeuMetHisX₀₁X₀₂X₀₃LysX₀₄AsnSerMetX₀₅ArgValGluTrpLeuArgLysLysLeuGlnAspValGluTrpLeuArgLysLysLeuGlnAspValGluTrpLeuArgLysLysLeuGlnAspValGluTrpLeuArgLysLysLeuGlnAspValGluTrpLeuArgLysLysLeuGlnAspValGluTrpLeuArgLysLysLeuGlnAspValGluTrpLeuArgLysLysLeuGlnAspValHis (SEQ ID NO:31) wherein:

X₀₁ is Ala, Asp or Gln;

 X_{02} is Leu, Arg or homoArg;

 X_{03} is Arg or Ala;

 X_{04} is Phe or Trp; and

 X_{05} is Arg or Ala.

- 6. (withdrawn) A polypeptide having an amino acid sequence that is at least 90% identical to the amino acid sequence of the polypeptide of claim 5.
- 7. (withdrawn) A polypeptide having an amino acid sequence selected from the group of sequences consisting of: AlaValAlaGluIleGlnLeuMetHisAlaArgAlaLysHis (SEQ ID No:3), AlaValSerGluIleGlnLeuMetHisAsnArgGlyLysHis (SEQ ID No:4), AlaValSerGluIleGlnLeuMetHisAsnArgAlaLysHis (SEQ ID No:5), AlaValAlaGluIleGlnLeuMetHisAsnArgAlaLysHis (SEQ ID No:6), AlaValAlaGluIleGlnLeuMetHisAlaArgAlaLysTrp (SEQ ID No:6), AlaValAlaGluIleGlnLeuMetHisAlaArgAlaLysTrp (SEQ ID No:6)

- No:7), AlaValAlaGluIleGlnLeuMetHisGlnArgAlaLysHis (SEQ ID No:8), AlaValAlaGluIle GlnLeuMetHisAlaArgAlaLys (SEQ ID No:9), AlaValAlaGluIleGlnLeuMetHisAlaArgAla (SEQ ID No:10), AlaValAlaGluIleGlnLeuMetHisAlaArg (SEQ ID No:11), AlaValAlaGluIle GlnLeuMetHisAlaArgAlaLysHisLeuAsnSerMetGluArgValGluTrpLeuArgLysLysLeuGln AspValHisAspTyr (SEQ ID No:12) and AlaValSerGluIleGlnLeuMetHisAlaArgAlaLysHis (SEQ ID No:13), AlaValAlaGluIleGlnLeuMetHisAlaArgAlaLysHisLeuAlaSerValGluArg MetGlnTrpLeuArgLysLysLeuGlnAspValHisAspTyr (SEQ ID No:20), AlaValAlaGluIleGln LeuMetHisAlaArgAlaLysHisLeuAsnSerMetGluArgValGluTrpLeuArgLysLysLeuGlnAsp ValHisAspTyr (SEQ ID No:22), AlaValAlaGluIleGlnLeuMetHisAlaArgAlaLysHisLeuAla SerValArgArgMetGlnTrpLeuArgLysLysLeuGlnAspValHisAspTyr (SEQ ID No:23) AlaVal AlaGluIleGlnLeuMetHisAlaArgAlaLysHisLeuArgLysLysLeuGlnAspValHisAspTyr (SEQ ID No:24)
- 8. (previously presented) The biologically active polypeptide of claim 1, wherein said polypeptide contains a C-terminal amide.
 - 9. (cancelled).
- 10. (currently amended) The biologically active polypeptide of claim 1 wherein said peptide is labeled with a label selected from the group consisting of: a radiolabel, a fluorescent label, a bioluminescent label, or a chemiluminescent label.
- 11. (currently amended) The biologically active polypeptide of claim 10, wherein said radiolabel is ^{99m} Tc.

- 12. (currently amended) A pharmaceutical composition comprising: the biologically active polypeptide of claim 1; and a pharmaceutically acceptable carrier.
- 13. (withdrawn) An isolated nucleic acid molecule comprising a nucleotide sequence encoding the polypeptide of claim 1.
- 14. (withdrawn) An isolated nucleic acid molecule comprising a nucleotide sequence encoding the polypeptide of claim 7.
- 15. (withdrawn) A recombinant DNA molecule comprising: (1) an expression control region, said region operably linked to (2) a polynucleotide sequence coding for the polypeptide of claim 1.
- 16. (withdrawn) A method of preparing a polypeptide, comprising introducing the nucleic acid of claim 13 into a host and expressing the polypeptide encoded by said nucleic acid.
- 17. (withdrawn) A method for making a recombinant vector comprising inserting a nucleic acid molecule of claim 13 into a vector.
- 18. (withdrawn) The recombinant DNA molecule of claim 15, wherein said control region includes a bacterial, viral, fungal or mammalian promoter.
- 19. (withdrawn) A prokaryotic or eukaryotic host cell containing the recombinant DNA molecule of claim 15.
 - 20. (withdrawn) The cell of claim 19 which is bacterial.

- 21. (withdrawn) The cell of claim 19 which is a yeast cell or a mammalian cell.
- 22. (withdrawn) A polypeptide having the amino acid sequence of SEQ ID NO:14, wherein a single amino acid substitution reduces cAMP stimulation relative to the native PTH in HKRK-B7 cells, provided that said substitution is not alanine at any position, the substitution at Ser-1 is not Tyr, Pro or Asp, the substitution at Val-2 is not Leu, Ser, Arg or Glu, the substitution at Ser-3 is not Thr, Gly, Ile, or Asn and the substitution at Glu-4 is not Gly, His, Lys, Val or Asp.
- 23. (withdrawn) A polypeptide having the amino acid sequence of SEQ ID NO:14, wherein a single amino acid substitution increases cAMP stimulation in HKRK-B7 cells relative to the native PTH polypeptide, provided that said substitution is not alanine.
- 24. (withdrawn) The polypeptide of claim 21 wherein said single amino acid substitution is selected from the group consisting of:
 - (a) Asn-10 -->Asp, Glu or Gln;
 - (b) Leu-11 --> Ile, Met, Lys, Arg or Trp;
 - (c) Gly-12 --> Arg or His;
 - (d) Lys-13 -->Leu, Arg, His or Trp; and
 - (e) His-14 -->Leu, Arg, Phe or Trp.
- 25. (withdrawn) The polypeptide of claim 21, wherein said polypeptide contains amino acids 1-9, 1-10, 1-11, 1-12 or 1-13.
- 26. (withdrawn) A polypeptide selected from the group consisting of: PTH (1-20), PTH (1-22), PTH (1-24), PTH (1-26), PTH (1-28), PTH (1-30), PTH (1-32) and PTH(1-34),

wherein a single amino acid substitution increases cAMP stimulation in HKRK-B7 cells relative to the native PTH polypeptide, provided that said substitution is not alanine.

- 27. (withdrawn) The polypeptide of claim 25 wherein said single amino acid substitution is selected from the group consisting of:
 - (a) Asn-10 -->Asp, Glu or Gln;
 - (b) Leu-11 --> Ile, Met, Lys, Arg or Trp;
 - (c) Gly-12 --> Arg or His;
 - (d) Lys-13 -->Leu, Arg, His or Trp; and
 - (e) His-14 -->Leu, Arg, Phe or Trp.
 - (f) Glu-19 -->Arg
- 28. (withdrawn) The polypeptide of claim 21, wherein said polypeptide contains amino acids 1-9, 1-10, 1-11, 1-12, 1-13, 1-14, 1-20, 1-22, 1-24, 1-26, 1-28, 1-30, or 1-32.
- 29. (withdrawn) A method for treating mammalian conditions characterized by decreases in bone mass, wherein said method comprises administering to a subject in need thereof an effective bone mass-increasing amount of the polypeptide of any one of claims 1.
- 30. (withdrawn) A method for determining rates of bone reformation, bone resorption and/or bone remodeling comprising administering to a patient an effective amount of a polypeptide of any one of claims 1 and determining the uptake of said peptide into the bone of said patient.

- 31. (withdrawn) The method of claim 29, wherein said effective bone mass-increasing amount of said peptide is administered by providing to the patient DNA encoding said peptide and expressing said peptide *in vivo*.
- 32. (withdrawn) The method of claim 29, wherein the condition to be treated is osteoporosis.
- 33. (withdrawn) The method of claim 32, wherein said osteoporosis is old age osteoporosis.
- 34. (withdrawn) The method of claim 32, wherein said osteoporosis is post-menopausal osteoporosis.
- 35. (withdrawn) The method of claim 29, wherein the effective amount of said polypeptide for increasing bone mass is from about 0.01 μg/kg/day to about 1.0 μg/kg/day.
- 36. (withdrawn) The method of claim 29, wherein the method of administration is parenteral.
- 37. (withdrawn) The method of claim 29, wherein the method of administration is subcutaneous.
- 38. (withdrawn) The method of claim 29, wherein the method of administration is nasal insufflation.
- 39. (withdrawn) A method of increasing cAMP in a mammalian cell having PTH-1 receptors, comprising contacting said cell with a sufficient amount of the polypeptide of claim 1 to increase cAMP in said cell.

40. (withdrawn) A polypeptide having the amino acid sequence AlaValAlaGluIleGln LeuMetHis $X_{01}X_{02}X_{03}$ Lys X_{04} LeuAsnSerMetGluArgValGluTrpLeuArgLysLysLeuGlnAspVal HisAsp X_{05} (SEQ ID NO:16) or SerValAlaGluIleGlnLeuMetHis $X_{01}X_{02}X_{03}$ Lys X_{04} LeuAlaSer ValGluMetGlnGluTrpLeuArgLysLysLeuGlnAspValHisAsp X_{05} (SEQ ID NO:21), wherein X_{01} is Ala Asp;

X₀₂ is Leu or Arg;

X₀₃ is Arg or Ala; X₀₄ is Phe or Trp; and

 X_{05} is Phe or Tyr.

41. (withdrawn) A method of increasing inositol phosphate in a mammalian cell having PTH-1 receptors, comprising contacting said cell with a sufficient amount of the polypeptide of claim 1 to increase inositol phosphate in said cell.

42. (currently amended) A biologically active polypeptide having an amino acid sequence, said sequence consisting essentially of a sequence selected from the group consisting of:

- (a) AlaValAlaGluIleGlnLeuMetHis $X_{01}X_{02}X_{03}$ Lys X_{04} (SEQ ID NO:1);
- (b) N- or C- derivatives thereof; and
- (c) fragments containing amino acids 1-9, 1-10, 1-11, 1-12 or 1-13 thereof;

wherein:

 X_{01} is Ala, Asp or Gln;

X₀₂ is Leu, Arg or homoArg;

 X_{03} is Arg or Ala; and

X₀₄ is Phe or Trp;

and wherein said polypeptide has a biological activity substantially similar to the biological activity of parathyroid hormone.